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Declaration under Rule 4.17:

as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, Fl, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

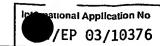
(54) Title: DIAGNOSTICS AND THERAPEUTICS FOR DISEASES ASSOCIATED WITH HUMAN PHOSPHODIESTERASE 11A (PDE11A)

(57) Abstract: The invention provides a human PDE11A which is associated with the disorders of the peripheral and central nervous system (Alzheimer), cardiovascular diseases, cancer (thyroid tumor, lung tumor, colon tumor), liver disease (liver cirrhosis) and genito-urinary diseases. The invention also provides assays for the identification of compounds useful in the treatment or prevention of disorders of the peripheral and central nervous system, cardiovascular diseases, cancer, liver disease and genito-urinary diseases. The invention also features compounds which bind to and/or activate or inhibit the activity of PDE11A as well as pharmaceutical compositions comprising such compounds.



VO 2004/029617

INTERNATIONAL SEARCH REPORT



A. CLASSIFICATION OF SUBJECT MATTER IPC 7 G01N33/574 C12Q1/44 A61K38/00

G01N33/68

A61K39/395

A61K48/00

Relevant to claim No.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Category °

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 GO1N C12Q C12N

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, WPI Data, BIOSIS, EMBASE, Sequence Search

Citation of document, with indication, where appropriate, of the relevant passages

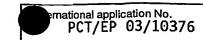
х	US 6 416 991 B1 (LANFEAR JERRY 9 July 2002 (2002-07-09) column 24, line 21 - column 25, claims 6,7; figures 5A,5B,7; ex	, line 44;	1-26	
х	EP 0 967 284 A (PFIZER LTD ;PF) 29 December 1999 (1999-12-29) paragraphs [0058] - [0066], [0 0364]; claims 10-22	IZER (US)) 9352], -/	1-26	
	•		• •	
X Furth	er documents are listed in the continuation of box C.	X Patent family members are listed in	n annex.	
Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed		"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention. "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone. "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family		
	March 2004	Date of mailing of the International sear	ch report 3. 04. 2004	
Name and n	nailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	. Authorized officer Vadot-Van Geldre,	Е	
Form PCT/ISA/2	(10 (second sheet) (January 2004)			



tional Application No PCT/EP 03/10376

		PCT/EP 03/10376
	ntion) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with Indication, where appropriate, of the relevant passages	Relevant to claim No.
Х	YUASA KEIZO ET AL: "Identification of rat cyclic nucleotide phosphodiesterase 11A (PDE11A). Comparison of rat and human PDE11A splicing variants" EUROPEAN JOURNAL OF BIOCHEMISTRY, BERLIN, DE, vol. 268, no. 16, August 2001 (2001-08), pages 4440-4448, XP002196953 ISSN: 0014-2956 figure 5; table 2	1-26
X	WO 01/66716 A (HARUOKA MOTOKO ;KAWABATA AYAKO (JP); MIYAJI HIROMASA (JP); NAKAMUR) 13 September 2001 (2001-09-13) abstract; figure 9	1-26
A	PEREZ-TORRES S ET AL: "Cellular expression of cAMP phosphodiesterase PDE4A, PDE4B and PDE4D mRNAs in Alzheimer's disease brains" SOCIETY FOR NEUROSCIENCE ABSTRACTS, vol. 27, no. 1, 2001, page 1134, XP002271232 31st Annual Meeting of the Society for Neuroscience; San Diego, California, USA; November 10-15, 2001 ISSN: 0190-5295 abstract	1-26
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Box I Observ	ations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This International	Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X Claims No because	los.: they relate to subject matter not required to be searched by this Authority, namely:
body,	ough claim 26 is directed to a method of treatment of the human/animal, the search has been carried out and based on the alleged effects of the bund/composition.
an exten	Nos.:
300 .	
3. Claims No because	Nos.: they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observ	rations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International	Searching Authority found multiple inventions in this international application, as follows:
see a	additional sheet
1. As all re searcha	quired additional search fees were timely paid by the applicant, this International Search Report covers all ble claims.
	earchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment dditional fee.
3. As only covers of	some of the required additional search fees were timely paid by the applicant, this International Search Report only those claims for which fees were paid, specifically claims Nos.:
	uired additional search fees were timely paid by the applicant. Consequently, this International Search Report is ed to the invention first mentioned in the claims; it is covered by claims Nos.: ms 1-26 (all partially)
Remark on Prot	The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claim 26 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.2

Claims Nos.: -

Present claims 19-21,24-26 relate to a pharmaceutical compositions, their production and their use defined by reference to a desirable characteristic or property, namely binding to or regulating the activity of a PDE11A polypeptide/polynucleotide. No true technical characterization is given.

The claims cover all pharmaceutical compositions, their production and their use having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT or disclosure within the meaning of Article 5 PCT for only a very limited amount of such pharmaceutical compositions. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT).

An attempt is made to define the pharmaceutical compositions, their production and their use by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, search has been carried out for those parts of the claims which appear to be clear and supported, namely those parts relating to the examples (antisense oligonucleotide, antibody).

Present claims 1-26 relate also to an extremely large number of possible diseases. In fact, the terms used to identify the different diseases are so broad and vague that a lack of clarity (and/or consiseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear (and/or consice), namely the relationship between PDE11A and specific diseases/tissues, based on table 1.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase

	International Application No. PCT/ EP 03/10376
FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210	
before the EPO, the applicant is reminded to out during examination before the EPO (see should the problems which led to the Articl overcome.	hat a search may be carried EPO Guideline C-VI, 8.5), e 17(2) declaration be

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: claims 1-26 (all partially)

PDE11A in methods for screening for therapeutic agents useful in the treatment of disorders of the peripheral and central nervous system (particularly as disclosed on pg 56 (lines 9-12), in methods of diagnosis of said diseases, pharmaceutical compositions containing therapeutic agents for the treatment of said diseases, their production and their use

2. claims: claims 1-26 (all partially)

PDE11A in methods for screening for therapeutic agents useful in the treatment of cardiovascular diseases (particularly as disclosed on pg 58 (lines 17-18), in methods of diagnosis of said diseases, pharmaceutical compositions containing therapeutic agents for the treatment of said diseases, their production and their use

3. claims: claims 1-26 (all partially)

PDE11A in methods for screening for therapeutic agents useful in the treatment of cancer (particularly as disclosed on pg 63 (lines 4-11), in methods of diagnosis of said diseases, pharmaceutical compositions containing therapeutic agents for the treatment of said diseases, their production and their use

4. claims: claims 1-26 (all partially)

PDE11A in methods for screening for therapeutic agents useful in the treatment of liver disease (particularly as disclosed on pg 60 (lines 6-7), in methods of diagnosis of said diseases, pharmaceutical compositions containing therapeutic agents for the treatment of said diseases, their production and their use

5. claims: claims 1-26 (all partially)

PDE11A in methods for screening for therapeutic agents useful in the treatment of genitological diseases (particularly as disclosed on pg 59 (lines 13), in methods of diagnosis of said diseases, pharmaceutical compositions containing therapeutic agents for the treatment of said diseases, their production and their use

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

6. claims: claims 1-26 (all partially)

PDE11A in methods for screening for therapeutic agents useful in the treatment of urological diseases (particularly as disclosed on pg 59 (line 13), in methods of diagnosis of said diseases, pharmaceutical compositions containing therapeutic agents for the treatment of said diseases, their production and their use

INTERNATIONAL SEARCH REPORT

International Application No
/EP 03/10376

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
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EP 0967284	Α	29-12-1999	EP JP US US	0967284 A1 2000023682 A 2002115176 A1 2004018542 A1	29-12-1999 25-01-2000 22-08-2002 29-01-2004
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